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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/016,159	01/30/1998	JONG Y. LEE	07004-002004	6621

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FISH & RICHARDSON P.C., P.A.
60 SOUTH SIXTH STREET
SUITE 3300
MINNEAPOLIS,, MN 55402

EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	

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35

Please find below and/or attached an Office communication concerning this application or proceeding.

Copy

Office Action Summary	Application No. 09/016,159	Applicant(s) JONG Y. LEE
	Examiner Fozia Hamud	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 10, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above, claim(s) *1, 2, and 7* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *3-6 and 8-10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 September 2002 in Paper No:34 has been entered.

Claims 1-10 are pending. Claims 1, 2, and 7 are withdrawn from consideration by the Examiner as they are drawn to non-elected inventions. Thus, claims 3-6 and 8-10 are under consideration by the Examiner.

2. The following previous rejections and objections are withdrawn in light of Applicants amendments filed in Paper No.34, 09/10/02:

(I) The rejection of claims 3, 5, 8-10, under 35 U.S.C §112, first paragraph for containing new matter.

(ii) The rejection of claims 4, 8 made under 35 U.S.C §102 (b), as being anticipated by Harris et al.

Claim objections:

3. Claims 3-6 and 8-10 are objected to because of the following informalities: some of the claims of the instant Application have been amended, however, there is no reflection of any amendments made to the claims. Applicant must convey the number of times each claim has been

amended, by placing said number within parenthesis, for example (once amended) or (twice amended).

Claim rejections-Double patenting

Non-statutory double patenting rejection (obviousness-type)

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4a. Claims 3 and 5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 4 of U.S. Patent No. 5,843,726. Although the conflicting claims are not identical, they are not patentably distinct from each other. Instant claim 3 is drawn

to a fusion protein consisting of an upstream portion, a cleavage site and extracellular domain of human EPO receptor polypeptide and instant claim 5 is drawn to a composition comprising said protein and a solid phase immunoassay reagent. Claim 4 of U.S. Patent No. 5,843,726 (having one common inventor with the instant application), is drawn to a purified fusion protein consisting of a first polypeptide segment, a thrombin cleavage site and a second polypeptide segment consisting of about amino acid 25 to 250 of full length human EPO receptor, (extracelluar domain). Claim 4 of the patent is species to claim 3 of the instant application which encompasses the subject matter of the patented claim, because the patented claim recites a specific cleavage site, (i.e a thrombin cleavage site). The patent claim is obvious from instant claim because the instant application is directed to genus subject matter, a purified fusion protein consisting of an upstream portion, a cleavage site and the extracelluar domain of human EPO, in which the patented claim is one specific embodiment. The infringement of the patented claim, would also result in the infringement of the broad claim of the instant application. Allowance of the pending claims, therefore, would have the effect of extending the enforceable life of the allowed claims beyond statutory limit.

Claim Rejections - 35 U.S.C. § 102 (b).

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5a. The rejection of claims 3, 5 made under 35 U.S.C. §102(b) as being anticipated by Harris et al. (JBC, 1992) is maintained for reasons of record as set forth in the office action of 26 September 2000, bottom of page 3.

(Claim 3 is interpreted as being drawn to the fusion protein and not to the extracelluar domain of EPO after it is cleaved). Applicants argue that Harris et al teach the production of a fusion

protein containing the extracellular domain of EPO receptor, however, Harris loses most of the protein product into non-functional, insoluble pellet, thereby not successfully producing high levels of the active peptide. Applicants also argue that antibodies of the present invention are directed against only the extracellular domain of the EPO, while Harris's antibodies are to the GST fusion protein.

Applicants' first argument is not persuasive, because Harris teaches a fusion protein that consists of an upstream portion (glutathione-transferase), a cleavage site and the extracellular domain of EPO receptor, and purifies said fusion protein. Harris et al also describe the immobilization of the extracelluar domain of EPO receptor on glutathione-agarose beads. The fusion protein taught by Harris et al is not distinguished from the claimed fusion protein, because it comprises an upstream portion, a cleavage site and the extracellular domain of EPO receptor. The fact that the claimed fusion protein is expressed at high levels, while Harris's may be lost in an insoluble pellet is irrelevant, because this does not change the structural requirement of the claimed fusion protein. Thus Harris et al anticipates instant claims 3 and 5, because it meets all of the structural limitations recited in said claims.

Applicants' second argument is persuasive, because Harris et al produce antibodies to the fusion not to the extracellular domain of EPO receptor. Therefore, the rejection of claims 4, 8 made under 35 U.S.C §102 (b), as being anticipated by Harris et al is withdrawn.

Claim Rejections - 35 U.S.C. § 102(a)

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6a. Claims 4, 6 and 10 are rejected under 35 U.S.C. §102(a) as being anticipated by Elliot et al (JBC 1996).

Elliot et al disclose antibodies raised to the extracellular domain of human EPO receptor, (see abstract, table 1). The researchers immunized mice by subcutaneously injecting them with soluble EPO receptor, collected the spleens and purified antibodies specific for extracelluar domain of human EPO receptor, screened them in ELISA, using ELISA plates that were coated with EPO-R extracelluar domain, and demonstrated that these antibodies were immunoreactive to EPO receptor, (see page 24692, column 1).

Thus the antibodies disclosed in Elliot et al reference meets all the limitations recited in claims 4, 6 and 10, because these antibodies are raised against the extracelluar domain of human EPO-receptor in a mammal (claims 4 and 10) and are bound to an ELISA plate (claim 6).

Therefore, Elliot et al reference anticipates instant claims 4, 6 and 10, because it meets all of the structural limitations recited in said claims.

Claim Rejections - 35 U.S.C. § 103

7. Claims 4, 6, 8, 9 and 10 are rejected under 35 U.S.C. §103 as being unpatentable over Harris et al. (JBC, 1992) in view of D'Andrea '808.

Harris et al teach a method of making and purifying antibodies by immunizing sheep with fusion protein comprising the extracelluar domain of human EPO-receptor. Harris et al also teach expressing the extracelluar domain of human EPO receptor in *E.coli* expression system, (see abstract and page 15206, column 2, second paragraph). However, Harris does not teach purified antibodies that are specific for the extracelluar domain of human EPO-receptor, an immunoassay composition

comprising said antibodies, or a method of obtaining antibodies only to the extracelluar domain of EPO receptor.

D'Andrea et al describe recombinant production and purification of extracelluar domain (secreted receptor) of the human EPO receptor, (see abstract and columns 17-21). D'Andrea also disclose the production of antibodies specific for the EPO receptor, (see column 3, lines 20-25). D'Andrea et al teach that the truncated form of the EPO receptor may be used as an affinity reagent for the identification, or purification of EPO, (columns 6-7).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made, to produce antibodies specific for the extracelluar domain of the human EPO-receptor, by immunizing sheep with the secreted form of the human EPO-receptor disclosed by D'Andrea et al, as taught by Harris et al.

With respect to claim 8, it would have been obvious to express the extracellular domain of the human EPO receptor in *E. Coli*, because Harris et al, teach that this an excellent expression system for the production and secretion of very high levels of biologically active proteins. One of ordinary skill in the art would have been motivated to make antibodies against the extracelluar domain of human EPO receptor, because antibodies to this domain would facilitate to conduct physiologic and functional studies of the EPO receptor, and to ascertain which of the biological activities of EPO is mediated by the extracelluar domain of the receptor.

Thus, the invention claimed in claims 4, 6, 8, 9 and 10 as a whole was obvious over the combined prior art.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 3 and 8 recite ".....capable of binding .. .. . " The specification is non-enabling for human EPO receptor polypeptide that does not bind to EPO and is only "capable of binding" it if further modified, since Applicants have not taught how to further modify the EPO receptor such that it can bind to EPO. It has been held that an element is "capable of" performing a function is not a positive limitation but only requires the ability to perform. It does not constitute a limitation in any patentable sense. In re Hutchison, 69 USPQ 138.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 3, 5, 6 and 9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9a. Claim 3 is vague and indefinite because it unclear whether the claim is drawn to the fusion protein, or to the free human erythropoietin extracellular domain. The structural limitation of the claim can not be ascertained, because once the fusion protein is purified and cut, the extracellular domain will be released, thus there will be no more fusion. Clarification of what s being claimed is required.

9b. Claims 5, 6 and 9 recite "..... *a solid phase immunoassay reagent....*", however, it is unclear what this phrase encompasses. There is no description of *a solid phase immunoassay reagent* in the instant specification, and thus the meets and bounds of the claims can not be ascertained. Appropriate correction is required.

Conclusion:

10. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursday from 6:30AM to 4:00PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
23 September 2002

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600